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MEHTA, ASHWIN D	
ART UNIT	PAPER NUMBER
1638	4

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/623,034	KLESSIG ET AL.
	Examiner	Art Unit
	Ashwin Mehta	1638

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-17 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-17 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No _____

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
4) ☐ Interview Summary (PTO-413) Paper No(s) _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Priority

1. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)).

Oath/Declaration

2. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

> The oath or declaration is defective because:
> It does not state that the person making the oath or declaration has reviewed and understands the contents of the specification, including the claims, as amended by any amendment specifically referred to in the oath or declaration.
>
> It does not state that the person making the oath or declaration acknowledges the duty to disclose to the Office all information known to the person to be material to patentability as defined in 37 CFR 1.56.

Specification

3. The specification fails to comply with the sequence rules, 37 CFR 1.821-1.825. Sequence identifiers should identify the amino acid sequences listed on page 32, line 5, and page 28, lines 30 and 31.

4. Figures 1-4 and 6-8 contain multiple parts, which are labeled with letters. The brief descriptions of these figures on pages 5-9 of the specification should start by referring to the parts of the figures. See 37 CFR 1.84. It is suggested, for example, that "Figure 1" in line 29 on page 5 be replaced with --Figure 1A-1B--.

Claim Objections

5. Claims 14-17 are objected to for the following minor informality: The recitation "which produces a transgenic plant having" in lines 1-2 of claim 14 should be replaced with --wherein the transgenic plant has--, to provide better structure. Similarly, the recitation "which produces a plant having" in lines 1-2 of claims 15-17 should be replaced with --wherein the transgenic plant has--.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "WIPK" in line 5 of claims 1 and 10, and line 2 of claims 2, 4, 6, 11-13 render the claims and those dependent thereon indefinite. The name "WIPK" does not clearly identify the enzyme or coding sequence referred to in the claims, and does not set forth the metes and bounds of the claimed invention. The name appears to be arbitrary and the specific

characteristics associated therewith could be modified. A tobacco WIPK cDNA taught by Seo et al. (Science, 1995, Vol. 270, pages 1988-1992) is exemplified in the instant specification (page 15, lines 28-31). Seo et al. designated their cDNA "WIPK," for "wound-induced protein kinase" (paragraph bridging pages 1988-1989). The instant specification continues to refer to this cDNA as "WIPK." However, the specification teaches that while the WIPK taught by Seo et al. is transiently induced at the mRNA level by wounding, there is little or no induction of WIPK protein, and that rather than being involved in wounding, WIPK protein is activatable in association with development or enhancement of resistance to microbial pathogens (page 4, lines 23-28; page 14, lines 19-25; page 36, lines 13-19). The specification teaches that WIPK- and SIPK- (salicylic acid-induced kinase) specific antibodies were used to determine that a 48 kD tobacco SIPK, and not the 44 kD WIPK encoded by the cDNA taught by Seo et al., is the wounding-activated kinase (page 36, lines 13-24). Given these teachings it is not clear that homologs of the cDNA taught by Seo et al. would be designated "WIPK". Further, Zhang et al. (Proc. Natl. Acad. Sci., USA, 1998, Vol. 95, pages 7225-7230) also call into question the designation of WIPK orthologs as wounding-activated kinases, and stress that further analysis is needed to firmly establish the relationship between these genes and the activated kinases (page 7229). Given this apparent confusion in the art concerning the designation of the name "WIPK," it is not clear what enzymes and coding regions are encompassed by the instant claims.

Further regarding claim 1: line 4 recites the limitation "said cell". There is insufficient antecedent basis in the claim for this limitation.

In claims 11 and 12: the claims recite the limitation "WIPK protein" in line 2. There is insufficient antecedent basis for this limitation in the claim, or parent claim 10.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn towards a transgenic plant having enhanced resistance to any plant-disease causing agent selected from the group consisting of all viruses, fungi, bacteria, and nematodes, wherein a cell of the plant being stably transformed with an expressible DNA construct encoding any WIPK enzyme; or wherein the DNA comprises a WIPK-encoding region operably linked to a constitutive or inducible promoter; or wherein the DNA construct comprises any tobacco WIPK coding sequence; a method of making a transgenic plant, comprising transforming regenerable plant cells with a recombinant DNA construct encoding any WIPK enzyme and regenerating a transgenic plant having enhanced resistance to any disease; or wherein said plant produced by said method has enhanced resistance to plant pathogens selected from the group consisting of any plant virus, bacteria, fungus, and nematode.

The specification indicates that the sequence of the WIPK cDNA exemplified in the invention is reported in the prior art document of Seo et al. (Science, 1995, Vol. 270, pages 1988-1992; specification, page 15, lines 28-31). WIPK is a mitogen-activated protein (MAP)

kinase. The specification describes that the WIPK taught by Seo et al. (which is reported by Seo et al. as having a size of 46 kD, but in the instant specification as 44 kD) is activated by tobacco mosaic virus (TMV), and that WIPK activation is associated with systemic acquired resistance (page 31, line 1 to page 32, line 27; page 34, lines 25-35).

However, the specification does not describe transgenic plants transformed with DNA constructs encoding a WIPK enzyme other than a tobacco WIPK described by Seo et al. The specification does not describe the coding sequences of other tobacco WIPK enzymes or orthologs or homologs from other species. The specification does not describe those structural features of the WIPK of Seo et al. that correlate it with its function. Further, the designation of the cDNA taught by Seo et al. as encoding a wound-induced kinase is called into question, as its encoded protein is not produced upon wounding, and therefore apparently not involved in a wound-response (page 35, lines 2-26, and as discussed above). Given the apparent confusion of the designation of the enzyme of Seo et al., is it not clear that other DNA constructs encoding proteins designated as "WIPK" correlate with the function of the WIPK of Seo et al. The specification also indicates that homologs of WIPK may be identified by hybridization (page 18, lines 5-22). However, a method of isolating homologs does not describe the genes or cDNA encoding them. See Fiers v. Sugano 25 USPQ 2d (CAFC 1993) at 1606, which states that "[a]n adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself". Given the breadth of the claims encompassing transgenic plants transformed with DNA constructs encoding any WIPK from any source, lack of guidance of the specification

as discussed above, the specification fails to provide an adequate written description of the multitude of nucleic acid sequences encompassed by the claims.

8. Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a transgenic plant transformed with the WIPK coding sequence taught by Seo et al. that have enhanced resistance to tobamoviruses in N gene expressing plants, and fungi that produce elicitin, and a method of making said transgenic plant, does not reasonably provide enablement for transgenic plants transformed with any other WIPK coding sequence or transgenic plants with enhanced resistance to all virus, non-elicitin producing fungi, bacteria, and nematodes, and for methods of making transgenic plants with enhanced resistance to all diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are broadly drawn towards a transgenic plant having enhanced resistance to any plant-disease causing agent selected from the group consisting of all viruses, fungi, bacteria, and nematodes, wherein a cell of the plant being stably transformed with an expressible DNA construct encoding any WIPK enzyme; or wherein the DNA comprises a WIPK-encoding region operably linked to a constitutive or inducible promoter; or wherein the DNA construct comprises any tobacco WIPK coding sequence; a method of making a transgenic plant, comprising transforming regenerable plant cells with a recombinant DNA construct encoding any WIPK enzyme and regenerating a transgenic plant having enhanced resistance to any disease; or wherein said plant produced by said method has enhanced

resistance to plant pathogens selected from the group consisting of any plant virus, bacteria, fungus, and nematode.

The specification teaches that a 44 kD tobacco protein designated WIPK is induced in TMV-infected tobacco plants, and that kinase activity of the protein is also activated (page31, line 1 to page 34, line 27). The specification teaches that activation of this WIPK in the TMV infected plants is also dependent on the presence of the N resistance gene, is not dependent on salicylic acid, and is associated with systemic acquired resistance (SAR; page 34, lines 7-34). The specification also indicates that transgenic plants constitutively expressing WIPK, taught by Seo et al., had elevated levels of salicylic acid and pathogenesis-related proteins following wounding (page 37, lines 21-27). The specification also teaches that WIPK is activated by treatment with fungal elicitins derived from Phytophthora (page 38, lines 21-24).

However, the specification does not teach WIPK coding sequences that can be used to make the claimed plants other than that taught by Seo et al. As discussed above, the specification teaches that a 48 kD protein, rather than the WIPK taught by Seo et al., encodes a tobacco wound-activated kinase. The specification teaches that a WIPK-specific antibody, produced using a peptide from the N-terminus of the protein taught by Seo et al., bound a 44 kD peptide (reported as 46 kD by Seo et al.), and that while mRNA encoding this peptide was transiently induced upon wounding, the encoded protein was not (page 31, line 1 to page 32, line 27; page 35, lines 3-26). The specification teaches that WIPK- and SIPK- (salicylic acid-induced kinase) specific antibodies were used to determine that a 48 kD tobacco SIPK, and not the 44 kD WIPK encoded by the cDNA taught by Seo et al., is the wounding-activated kinase (page 36, lines 13-24). It is therefore unpredictable that transgenic plants transformed with

coding sequences for other proteins designated WIPK, which encode wound-activated kinases, would have enhanced resistance to disease-causing agents. Further, Zhang et al. (Proc. Natl. Acad. Sci., USA, 1998, Vol. 95, pages 7225-7230) call into question the designation of WIPK orthologs as wounding-activated kinases, and stress that further analysis is needed to firmly establish the relationship between these genes and the activated kinases (page 7229). In light of this confusion over the designation "WIPK", it is unpredictable what coding sequences are encompassed by the claims. It would require undue experimentation by one skilled in the art to determine whether not WIPK homologs known in the art are wound-activated kinases. Such kinases would not be encompassed by the claims, since the exemplified kinase of the invention, taught by Seo et al., is apparently not wound-activated, despite its name. The specification does not provide sufficient guidance for one to identify WIPKs that can be used with the invention, from those that cannot.

Further, the specification does not teach that the claimed invention confers protection against all viruses, and in all plants. As discussed, the specification teaches that activation of WIPK is dependent on the presence of the N gene. The N gene of tobacco confers resistance to TMV and other tobamovirus family members (Whitham et al., Proc. Natl. Acad. Sci., USA, 1996, Vol. 93, pages 8776-8781, see page 8776). As the N gene is known not to confer resistance to other types of viruses, it would require one skilled in the art undue experimentation, in the absence of further guidance, to determine how the claimed invention can be used to confer resistance to plants against non-tobamoviruses and in plants that do not produce the N gene.

The specification also does not provide any teaching at all showing that the claimed invention provides enhanced resistance against nematodes. Nematode infections can result in a

number of symptoms, such as root knots, root lesions, injured root tips, reduced growth, nutrient deficiencies, distortion of leaves, abnormal floral development (In Agrios, G., N., Plant Pathology, 2nd edition, 1978, page 619). The specification does not teach that any such symptoms are relieved by WIPK. Nematode feeding causes mechanical injury, however as discussed above, wounding does not induce WIPK protein expression or activation, and WIPK is not involved in the response to wounding. Given that neither the prior art nor the specification teach the relief of disease symptoms caused by nematodes, it would require undue experimentation by one skilled in the art to produce transgenic plants expressing a WIPK enzyme with enhanced resistance to nematodes. See Genentech, Inc. V. Novo Nordisk, A/S, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention.

The specification teaches that fungal elicitins from Phytophthora fungi activate WIPK (page 38, lines 21-24). However, examples of other stimulators of WIPK activation are lacking in the prior art, and not taught by the specification. The specification does not provide any suggestions as to what other stimulators may activate WIPK, and admits that WIPK is activated by only a subset of stresses that activate another MAP kinase, SIPK, including TMV infection and elicitin treatment (page 38, lines 21-24). As WIPK activation, not just WIPK expression, is required to practice the claimed invention, it is not clear how the claimed method would produce transgenic plants having enhanced resistance to diseases caused by pathogens that do not produce a stimulator that activates WIPK. In the absence of further guidance, it would require undue experimentation for one skilled in the art to determine what pathogens produce stimulators, other than tobamoviruses (in plants expressing the N gene), and elicitin-producing

Phytophthora. Given the breadth of the claims encompassing any DNA construct encoding any enzyme designated "WIPK" and methods producing transgenic plants with enhanced resistance to any disease and all viruses, fungi, bacteria, and nematodes, unpredictability of the art and lack of guidance of the specification as discussed above, undue experimentation would be required by one skilled in the art to make and use the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1-3, 6-11, and 13-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Seo et al. (Science, 1995, Vol. 270, pages 1988-1992).

The claims are broadly drawn towards a transgenic plant having enhanced resistance to any plant disease-causing agent selected from the group consisting of all viruses, fungi, bacteria, and nematodes, wherein a cell of the plant is stably transformed with an expressible DNA construct encoding any WIPK enzyme; or wherein the DNA comprises any WIPK-encoding region operably linked to a constitutive promoter; or wherein the DNA construct comprises any tobacco WIPK coding sequence; a method of making a transgenic plant, comprising transforming regenerable plant cells with a recombinant DNA construct encoding any WIPK enzyme and regenerating a transgenic plant having enhanced resistance to any disease; or wherein said plant produced by said method has enhanced resistance to plant

pathogens selected from the group consisting of any plant virus, bacteria, fungus, and nematode.

Seo et al. teach transgenic plants produced by transforming plants with a tobacco cDNA encoding a WIPK enzyme, operably linked to the constitutive CaMV 35S promoter, produced. Leaf disks were transformed, and transgenic plants recovered (pages 1989-1991). Enhanced resistance to disease caused by pathogens including tobacco mosaic virus, species of the fungal genus Phytophthora, and species of the bacterial genus Pseudomonas, is a property inherent to the transgenic plant.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seo et al. (Science, 1995, Vol. 270, pages 1988-1992) in combination with Gatz et al. (Mol. Gen. Genet., 1991, Vol. 227, pages 229-237).

The claims are broadly drawn towards a transgenic plant having enhanced resistance to any plant-disease causing agent selected from the group consisting of all viruses, fungi, bacteria, and nematodes, wherein a cell of the plant is stably transformed with an expressible DNA construct encoding any WIPK enzyme; or wherein the DNA comprises any WIPK-encoding region operably linked to a constitutive or inducible promoter; or wherein the inducible promoter is a tetracycline repressor/operator controlled promoter; or wherein the DNA construct comprises any tobacco WIPK coding sequence; a method of making a transgenic plant, comprising transforming regenerable plant cells with a recombinant DNA construct encoding any WIPK enzyme and regenerating a transgenic plant having enhanced resistance to any disease; or wherein said plant produced by said method has enhanced resistance to plant pathogens selected from the group consisting of any plant virus, bacteria, fungus, and nematode.

Seo et al. is discussed above.

Seo et al. do not teach inducible promoters.

Gatz et al. teach a Tn10-encoded tet repressor-operator system to regulate expression of an engineered CaMV 35S promoter in transgenic tobacco plants. Maximal induction of the promoter is achieved after 30 min. upon application of 0.1 mg/l tetracycline. Gatz et al. teach that the tet system is fast, efficient, and can be used for the regulation of integrated genes and for

specifically inducing expression of transferred genes at different stages of plant development (abstract, pages 231-234, 236).

It would have been obvious and within the scope of one of ordinary skill in the art at the time the invention was made to modify the production of transgenic plants expressing WIPK taught by Seo et al. by replacing the constitutive promoter an inducible promoter, including the tetracycline repressor/operator controlled promoter taught by Gatz et al. A wide variety of promoters are available in the art, which researchers routinely use to achieve a desired end. One would have been motivated to use the inducible tetracycline repressor/operator controlled promoter, given the speed, efficiency, and control it offers in controlling transgene expression, as taught by Gatz et al.

12. No claim is allowed.

Contact Information

Any inquiry concerning this communication from the examiner should be directed to Ashwin Mehta, whose telephone number is 703-306-4540. The examiner can normally be reached on Mondays-Thursdays and alternate Fridays from 8:00 A.M to 5:30 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at 703-306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 and 703-305-9306 for regular communications and 703-872-9307 for After Final communications. Any inquiry of a general nature or relating to the

status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

January 14, 2002

ASHWIN D. MEHTA, PH.D
PATENT EXAMINER